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iVIEW

EDITOR'S PAGE

À LA Mode Atrioventricular Mechanical Coupling

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Left atrial (LA) size and function have been popularized as barometers of left ventricular (LV) filling pressure and diastolic function. However, the specific role of the left atrium, independent of the left ventricle, and its clinical assessment remain challenging. Several recent investigations have suggested that measuring changes in LA volume (1), wall deformation (2), or the extent of wall fibrosis (3) may be clinically useful for predicting adverse cardiac events such as atrial fibrillation (AF) and mortality in patients with LV diastolic dysfunction. In this issue of *iJACC*, Neilan et al. (4) and the accompanying editorial (5) revisit the structural and functional tenets of atrioventricular coupling for understanding the rate-limiting pathophysiological features of patients with diastolic dysfunction that are finally associated with atrial arrhythmias.

LA function shows phasic variations during different periods of the cardiac cycle (1). The left atrium functions as a receiving and dilating chamber (*reservoir*) during ventricular systole, allowing uninterrupted flow to arrive into the atrium even when the mitral valve is closed. The flow from the left pulmonary veins enters the LA cavity (Fig. 1) and starts rotating along a crescent-like axis to parallel the C-shaped closure line of the mitral valve leaflets (6). In contrast, the flow from the right pulmonary veins travels separately along the LA wall, creating noncolliding streams of blood flow. These blood flow streams wash the LA surface, avoiding hemodynamic stasis and thrombus formation, while the LA reservoir expands to reach its maximal volume. One could surmise that the lack of an intervening atrial chamber would halt the forward movement of venous blood flow when the mitral valve is closed and let the kinetic energy of the moving blood convert to a surge of static pressure that might damage the pulmonary venous architecture during each ventricular systole. This shielding action of the dilating atria that sustains continuous forward blood flow in systole remains largely under appreciated.

The diastolic filling phases show more intricate hemodynamic interactions (1). In early diastole, blood flow rotation ceases in the left atrium as the body of blood drops into the LV cavity (*passive filling*) but contributes to the vortex formation inside the LV cavity. This early diastolic vortex in the LV cavity is stronger than flow rotation seen in the left atrium and ensures a buildup of kinetic energy that is used in expanding the left ventricle to a higher end-diastolic volume. Because the expansion of the left ventricle greatly exceeds the volume decompression of the left atrium, a large volume of blood is directly aspirated into the left ventricle from the pulmonary venous circulation (*conduit volume*). During the period of diastasis, the speed of transmitral flow is transiently reduced before the onset of atrial contraction (*active or booster filling*), which energizes the flow at the end of ventricular diastole and vortex formation. Flow vortex in the late diastole helps redirect LA flow toward the LV outflow region and has been suggested to help prime the left ventricle during pre-ejection (*we often call it a hoop-LA nudge*), stretching the cardiomyocytes for pre-load-related adjustments in LV shortening strains (*the Frank-Starling law*).

The presence of LV hypertrophy and diastolic dysfunction, as seen in patients with systemic hypertension, is associated with loss of early diastolic suction and decreased compliance. Increasing LV filling pressures prevent the left atrium from decompressing in early diastole (reduced LA passive emptying and conduit volume). The left atrium adapts by increasing the active LA emptying volume. In addition, chronic elevation of filling pressures creates more wall stress, which dilates the LA cavity, increasing both minimal and maximal LA volumes;

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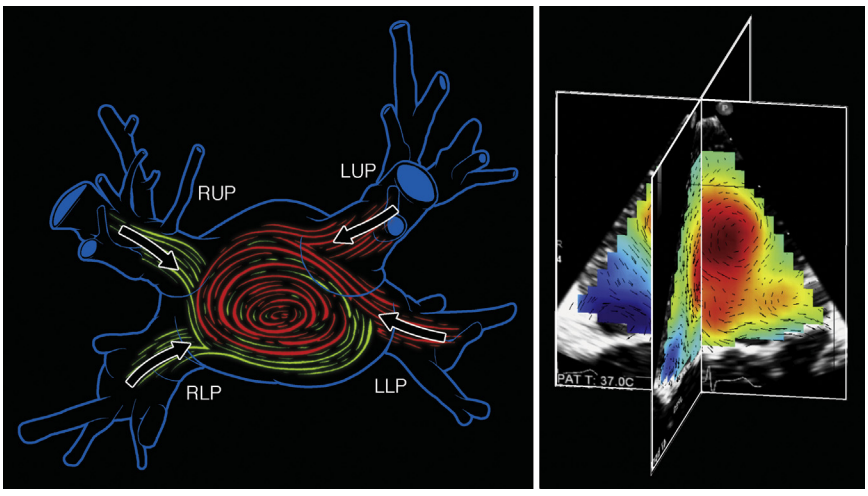

Figure 1. Left Atrial Flow During the Reservoir Phase

The schematic figure **(left)** shows the formation of counterclockwise vortex inside the left atrial cavity during ventricular systole (reservoir phase). Echocardiography contrast echo particle velocimetry performed on a biplane transesophageal view of the left atrium during the reservoir phase **(right)** also reveals the presence of a large transient counterclockwise rotation **(red)** in the left atrial flow. RUP, RLP, LUP, LLP denote right and left, upper and lower pulmonary veins.

a rise in LA minimal volume has been reported to be more reflective of the elevation of LV filling pressures. The increase in LA volume further increases wall stress and triggers myocyte hypertrophy and fibrosis. Growing evidence derived from both clinical and experimental studies suggests that patients with diastolic dysfunction show concurrent fibrotic remodeling of both LA and LV myocardium (2,7). The study by Neilan et al. (4) in this issue used cardiac magnetic resonance (CMR) imaging to demonstrate the association between CMR-derived extracellular myocardial volume expansion (*an index of LV fibrosis*) and the recurrence of AF after pulmonary vein ablation. LV fibrosis in patients with AF may be a reflection of the same process in the left ventricle that also leads to atrial fibrosis and AF and therefore may identify the pathologic myocardial process triggering AF recurrence. The modification in atrial architecture impedes normal atrial electrical conduction, creating an arrhythmogenic milieu. Given the presence of crosstalk between the cardiac chambers whereby LV fibrosis predicted the recurrence of AF demonstrated by Neilan et al. (4), future studies need to further explore the relative merits of assessing how CMR-derived LV fibrosis relates to the burden of atrial fibrosis and vice versa.

The presence of atrial tissue fibrosis can be expected to alter LA compliance and tissue properties. Indeed, patients with paroxysmal or persistent AF lose the ability to distend the left atrium, resulting in a loss of reservoir function and a reduction of LA reservoir function is an independent predictor of the occurrence of atrial arrhythmia (1). Speckle-tracking echocardiography has recently been used for the assessment of LA function. A reduction in LA strain during the reservoir phase precedes LA enlargement in patients with paroxysmal AF (8). LA strain also correlates with the risk for thromboembolism (9). It predicts AF occurrence after pulmonary vein ablation (3) and in the aftermath of cardiac surgery. Only a few studies have investigated the structural basis of the reduction in LA strain that correlates with the delayed-enhancement CMR–verified burden of LA wall fibrosis in patients with AF (10) and the histological extent of LA fibrosis measured in tissue samples obtained during cardiac surgery in patients with severe mitral regurgitation (11,12). These data suggest that the assessment of LA reservoir function using echocardiography provides an integrated assessment of structural and functional remodeling of the left atrium, including the extent of LA fibrosis.

Atrioventricular coupling is a dynamic and time-variant process. The fundamental loss of LA reservoir function (such as that assessed by speckle-tracking echocardiographic strain) identifies an advanced stage of LA remodeling compared with LA size alone and is closely associated with adverse

clinical events, including atrial arrhythmias, heart failure, and death. This stage probably can be morphologically characterized by the presence of CMR-verified LV fibrosis. Data from both techniques provide mechanistic insights into the same evolutionary scale and need to be compared to construct an accurate and cost-effective algorithm. With the current estimate that AF affects up to 2% of the entire population, with a projected doubling by 2050, better risk stratification and identification of the milieu associated with the evolution of AF may have profound social and economic implications.

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